SUPPLEMENTARY MATERIAL

Estimating the Impact of Delayed Access to Oncology Drugs on Patient Outcomes in Canada

Jackie Vanderpuye-Orgle PhD, MSc,[1] Daniel Erim MD, PhD, MSc,[1] Yi Qian PhD,[2] Devon J. Boyne PhD,[3,4] Winson Y. Cheung MD, MPH,[3,4] Gwyn Bebb, BMBCh, PhD,[2,3] Ariel Shah, MBA,[2] Louisa Pericleous, PhD,[5] Maciej Maruszczak, MSc,[6] Darren R. Brenner PhD[3,4]

[1] Advanced Analytics, HEOR and RWE, Parexel International, Billerica, MA, USA

[2] Amgen Inc, Thousand Oaks, CA, USA

[3] University of Calgary, Department of Oncology, Calgary, Alberta, Canada

[4] Oncology Outcomes (O2) Initiative, University of Calgary, Alberta, Canada

[5] Amgen Canada Inc, Mississauga, Ontario, Canada

[6] Advanced Analytics, HEOR and RWE, Parexel International, London, UK

Corresponding author: Dr Jackie Vanderpuye-Orgle

Email: Jackie.Vanderpuye-Orgle@parexel.com

Supplementary Table 1: CADTH-pCODR-approved indications for reimbursement of nivolumab, afatinib, and pemetrexed

Oncology drug	Indication approved for reimbursement
Nivolumab	Adults (age 18+ years) with advanced or metastatic (stage IIIB or IV or recurrent) squamous or non-squamous NSCLC with disease progression during or after cytotoxic chemotherapy for advanced disease and have a good performance status (ECOG 0, 1, possibly ≥ 2).
Afatinib	Adults (age 18+ years) with *EGFR* mutation-positive, advanced or metastatic (stage IIIB or IV or recurrent) squamous or non-squamous NSCLC (adenocarcinoma) with good performance status (ECOG 0, 1, possibly ≥ 2) as first-line treatment.
Pemetrexed	Maintenance therapy in adults (age 18+ years) following first-line treatment with pemetrexed and cisplatin for advanced or metastatic (stage IIIB or IV or recurrent) non-squamous NSCLC with ECOG performance status of 0 or 1 following induction with four cycles of pemetrexed plus cisplatin with good performance status (ECOG ≤ 1).

CADTH, Canadian Agency for Drugs and Technologies in Health; ECOG, European Cooperative Oncology Group; *EGFR*, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; pCODR, pan-Canadian Oncology Drug Review.

Supplementary Table 2: Estimates of median survival within clinical trials used as basis of evidence in CADTH-pCODR submissions

Metric/indicator	Nivolumab	Afatinib[a]	Pemetrexed
Comparator treatment	CM-057: Docetaxel CM-017: Docetaxel	LUX-Lung 3: Pemetrexed-cisplatin LUX-Lung 6: Gemcitabine-cisplatin LUX-Lung 7: Gefitinib	PARAMOUNT: Placebo
Median overall survival in active treatment arm	CM-057: 12.2 months CM-017: 9.2 months Pooled: 11.1 months	LUX-Lung 3: 28.2 months LUX-Lung 6: 23.6 months LUX-Lung 7: 27.9 months	PARAMOUNT: 16.9 months
Median overall survival in comparator treatment arm	CM-057: 9.4 months CM-017: 6.0 months Pooled: 8.1 months	LUX-Lung 3: 28.2 months Lux-Lung 6: 23.6 months LUX-Lung 7: 25.0 months	PARAMOUNT: 14.0 months
Absolute difference in median overall survival	CM-057: 2.8 months CM-017: 3.4 months	LUX-Lung 3: 4.2 months LUX-Lung 6: – Lux-Lung 7: 2.5 months	PARAMOUNT: 2.9 months
Increase in median survival relative to median survival in comparator arm [b]	CM-057: 29.8% CM-017: 56.7%	LUX-Lung 3: 0.0% LUX-Lung 6: -2.1% LUX-Lung 7: 11.6%	PARAMOUNT: 20.7%

[a] Note: the lack of difference in overall survival for LUX-Lung 3 and 6 likely due to treatment switching

[b] Estimated as follows: (median overall survival in active arm − median overall survival in control arm)/median overall survival in control arm.

CADTH, Canadian Agency for Drugs and Technologies in Health; pCODR, pan-Canadian Oncology Drug Review.

Supplementary Table 3: Breakdown of epidemiologic and economic impacts of delays in access to nivolumab on Canadian patients with NSCLC.

	Canadian NSCLC patients (2017)		**Patients affected by indicated delays**				**Epidemiologic & economic impacts**		**Economic value of QALYs lost**	
	Patients diagnosed	*Patients with appropriate indication*	*Health Canada*	*CADTH/ pCODR*	*Provincial authorities*	*Total*	*Person-years of life lost*	*QALYs lost*	*$50,000/QALY*	*$100,000/QALY*
Alberta	2200	203	0	7	18	25	8	4.8	$0.2 M	$0.5 M
British Columbia	3050	281	0	9	0	9	3	1.8	$0.1 M	$0.2 M
Manitoba	910	84	0	3	3	6	2	1.1	$0.1 M	$0.1 M
New Brunswick	710	66	0	2	11	13	4	2.6	$0.1 M	$0.3 M
Newfoundland and Labrador	540	50	0	2	21	23	7	4.4	$0.2 M	$0.4 M
Nova Scotia	950	88	0	3	7	10	3	2.0	$0.1 M	$0.2 M
Ontario	10,600	977	0	32	53	86	26	16.5	$0.8 M	$1.6 M
Prince Edward Island	135	13	0	0	18	19	6	3.6	$0.2 M	$0.4 M
Quebec	8700	802	0	0	31	31	9	5.9	$0.3 M	$0.6 M
Saskatchewan	790	73	0	2	4	7	2	1.3	$0.1 M	$0.1 M
Total	28,585	2637	0	61	169	229	70	44	$2.2 M	$4.4 M

CADTH, Canadian Agency for Drugs and Technologies in Health; M, million; NSCLC, non-small cell lung cancer; pCODR, pan-Canadian Oncology Drug Review; QALY, quality-adjusted life year. Submission to Health Canada was made pre-NOC (Notice of Compliance), thus any delay within Health Canada would overlap with the duration of review at CADTH/pCODR.

All costs are in CA$

Supplementary Table 4: Breakdown of epidemiologic and economic impacts of delays in access to afatinib, on Canadian patients with NSCLC.

	Canadian NSCLC patients (2014)		**Patients affected by indicated delays**				**Epidemiologic & economic impacts**		**Economic value of QALYs lost**	
	Patients diagnosed	*Patients with appropriate indication*	*Health Canada*	*CADTH/ pCODR*	*Provincial authorities*	*Total*	*Person-years of life lost*	*QALYs lost*	*$50,000/QALY*	*$100,000/QALY*
Alberta	2250	422	0	102	49	150	34	22.1	$1.1 M	$2.2 M
British Columbia	3185	597	0	144	70	214	48	31.6	$1.6 M	$3.2 M
Manitoba	930	175	0	42	28	70	16	10.3	$0.5 M	$1.0 M
New Brunswick	790	148	0	36	9	45	10	6.6	$0.3 M	$0.7 M
Newfoundland and Labrador	505	95	0	23	74	97	22	14.3	$0.7 M	$1.4 M
Nova Scotia	995	187	0	45	68	113	25	16.6	$0.8 M	$1.7 M
Ontario	8790	1646	0	397	0	397	89	58.4	$2.9 M	$5.8 M
Prince Edward Island	155	30	0	7	65	73	16	10.7	$0.5 M	$1.1 M
Quebec	8200	1535	0	0	2622	2622	586	386.5	$19.3 M	$38.6 M
Saskatchewan	740	139	0	33	10	44	10	6.4	$0.3 M	$0.6 M
Total	26,540	4974	0	829	2997	3825	855	564	$28.2 M	$56.4 M

CADTH, Canadian Agency for Drugs and Technologies in Health; M, million; NSCLC, non-small cell lung cancer; pCODR, pan-Canadian Oncology Drug Review; QALY, quality-adjusted life year. Submission to Health Canada was made pre-Notice of Compliance; thus, any delay within Health Canada would overlap with the duration of review at CADTH/pCODR.

All costs are in CA$

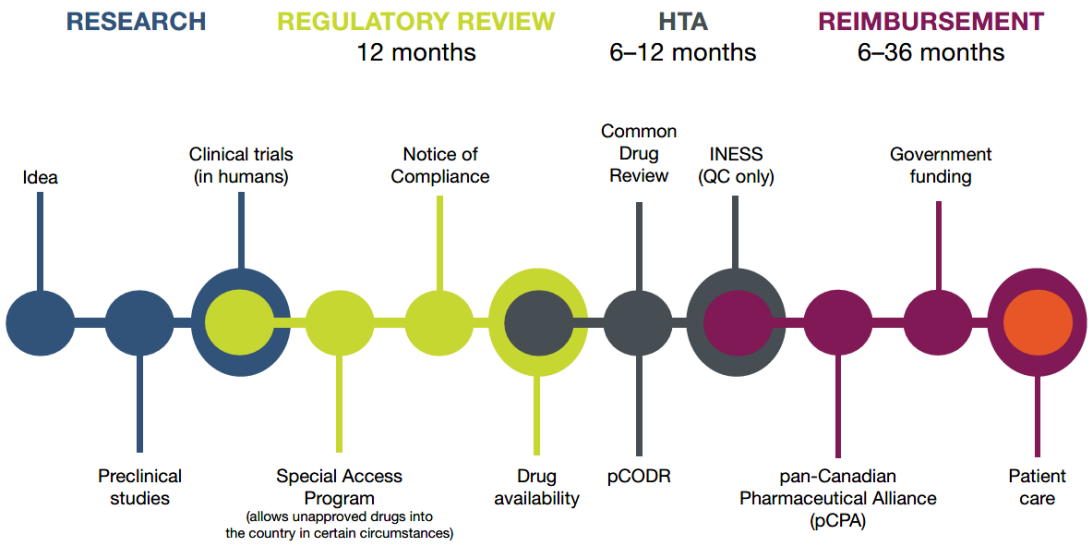
Supplementary Table 5: Breakdown of epidemiologic and economic impacts of delays in access to pemetrexed on Canadian patients with NSCLC.

	Canadian NSCLC patients (2014)		**Patients affected by indicated delays**				**Epidemiologic & economic impacts**		**Economic value of QALYs lost**	
	Patients diagnosed	*Patients with appropriate indication*	*Health Canada*	*CADTH/ pCODR*	*Provincial authorities*	*Total*	*Person-years of life lost*	*QALYs lost*	*$50,000/QALY*	*$100,000/QALY*
Alberta	2250	721	Unavailable	0	116	116	40	25.4	$1.3 M	$2.5 M
British Columbia	3185	1020	Unavailable	0	165	165	57	36.0	$1.8 M	$3.6 M
Manitoba	930	298	Unavailable	0	73	73	25	16.0	$0.8 M	$1.6 M
New Brunswick	790	253	Unavailable	0	126	126	44	27.5	$1.4 M	$2.8 M
Newfoundland and Labrador	505	162	Unavailable	0	13	13	4	2.8	$0.1 M	$0.3 M
Nova Scotia	995	319	Unavailable	0	25	25	9	5.5	$0.3 M	$0.6 M
Ontario	8790	2815	Unavailable	0	224	224	77	48.8	$2.4 M	$4.9 M
Prince Edward Island	155	50	Unavailable	0	86	86	30	18.8	$0.9 M	$1.9 M
Quebec	8200	2626	Unavailable	0	1524	1524	528	332.9	$16.6 M	$33.3 M
Saskatchewan	740	237	Unavailable	0	0	0	0	0.0	$0.0 M	$0.0 M
Total	26,540	8501	Unavailable	0	2353	2353	816	514	$25.7 M	$51.4 M

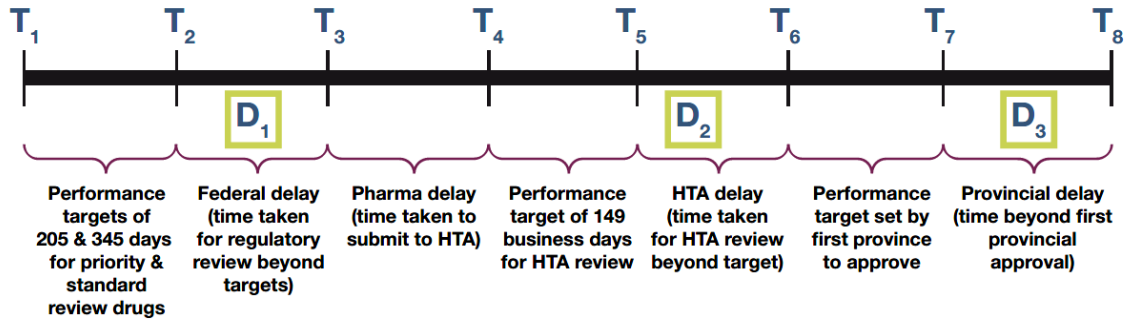
CADTH, Canadian Agency for Drugs and Technologies in Health; M, million; NSCLC, non-small cell lung cancer; pCODR, pan-Canadian Oncology Drug Review; QALY, quality-adjusted life year.

All costs are in CA$

Supplementary Figure 1 (Panel A): Current drug approval and funding process in Canada



Supplementary Figure 1 (Panel B): Sources of delayed access considered

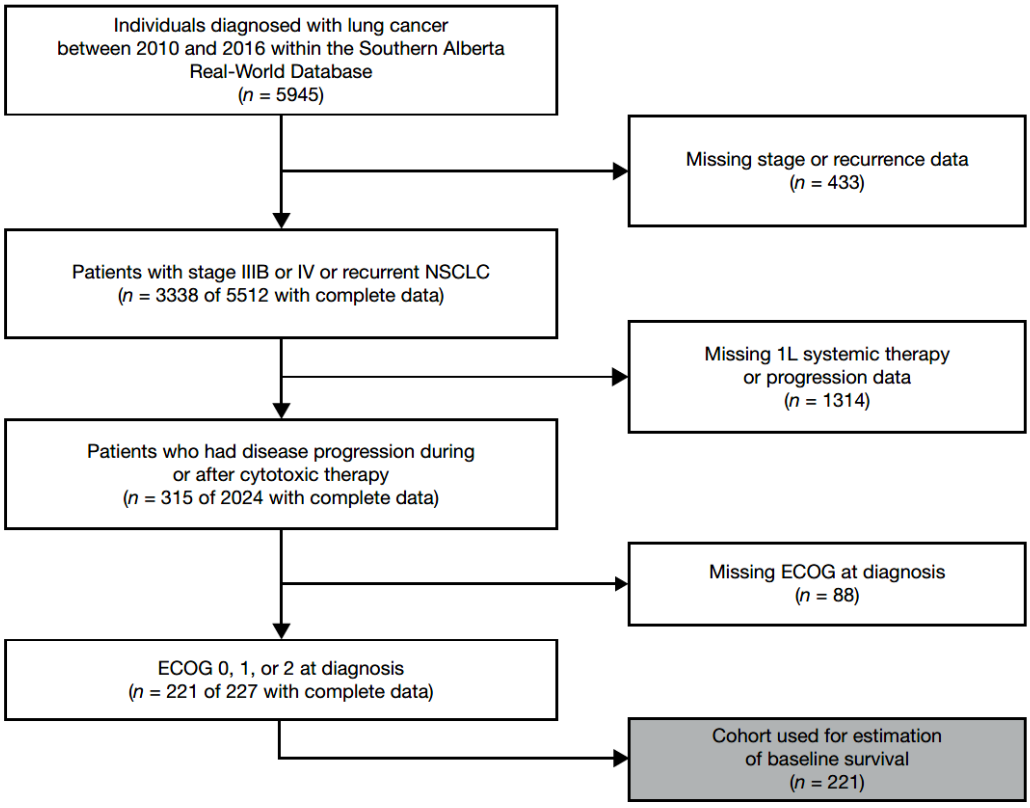


- T_1 = Date of submission to Health Canada
- T_2 = Performance benchmarks
- T_3 = Notice of Compliance (NOC) from Health Canada
- T_4 = Date of submission to CADTH-pCODR
- T_5 = Performance benchmark
- T_6 = Notification to Implement (NOI) from CADTH-pCODR
- T_7 = First province approves for reimbursement
- T_8 = Subsequent provinces approve

- D_1 = Federal delay
- D_2 = HTA delay
- D_3 = Provincial delay

CADTH, Canadian Agency for Drugs and Technologies in Health; HTA, health technology assessment; INESS, Institut National d'Excellence en Santé et en Services Sociaux; pCODR, CADTH pan-Canadian Oncology Drug Review.

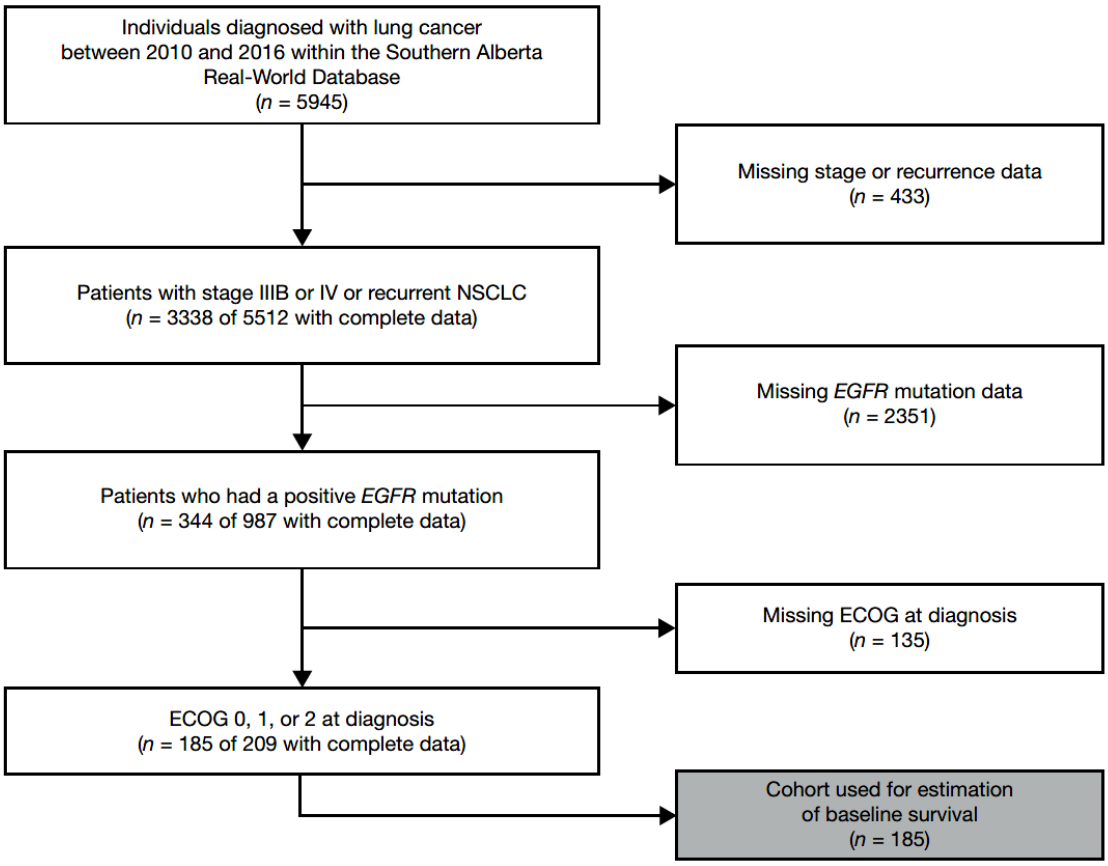
Supplementary Figure 2: Identification of patients eligible for nivolumab in the Southern Alberta Lung Cancer database



1L, first line; ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer.

The proportion of NSCLC patients with an appropriate indication for nivolumab was estimated thus: (3338/5512)×(315/2024)×(221/227) = 9.2%. Median overall survival was estimated using survival data from 221 patients in the indicated cohort.

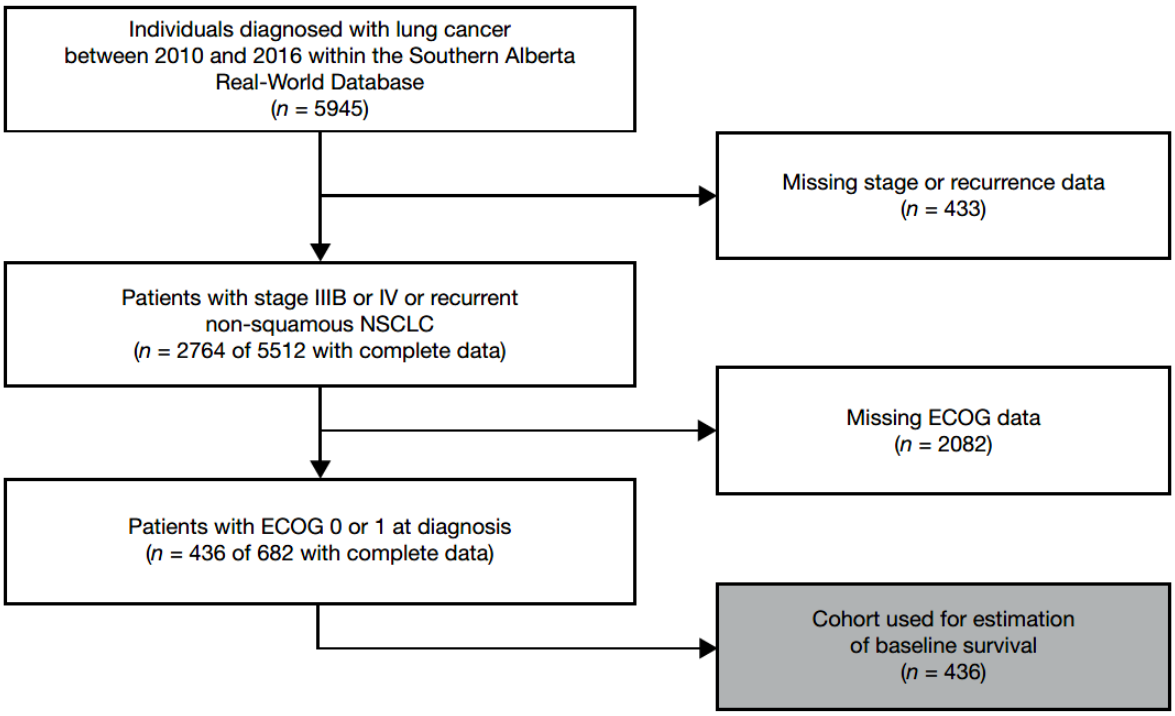
Supplementary Figure 3: Identification of patients eligible for afatinib in the Southern Alberta Lung Cancer database



ECOG, Eastern Cooperative Oncology Group; *EGFR*, epidermal growth factor receptor; NSCLC, non-small cell lung cancer.

The proportion of NSCLC patients with appropriate indication for afatinib was estimated thus: (3338/5512)×(344/987)×(185/209) = 18.7%. Median overall survival was estimated using survival data from 185 patients in the indicated cohort.

Supplementary Figure 4: Identification of patients eligible for pemetrexed in the Southern Alberta Lung Cancer database



ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer.

The proportion of NSCLC patients with appropriate indication for pemetrexed was estimated thus: (2764/5512)×(436/682)=32.0%. Median overall survival was estimated using survival data from 436 patients in the indicated cohort.